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EXAMINER

SHAFFER, SHULAMITH H

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 09/965,697	Applicant(s) DHADIALLA ET AL.	
	Examiner SHULAMITH H. SHAFER	Art Unit 1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 April 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4, 7-12, 15, 21-46, 48 and 49 is/are pending in the application.
- 4a) Of the above claim(s) 21-46 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4, 7-12, 15, 48 and 49 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>10/15/08</u> . | 6) <input type="checkbox"/> Other: _____ |

Detailed Action

Status of Application, Amendments, And/Or Claims:

Applicant's response, of 7 April 2009, is acknowledged and has been entered. Claim 47 has been canceled. Claims 1, 2, 4, 9, 10 and 12 have been amended and the amendment made of record. Claims 48 and 49 are newly presented and made of record.

Claims 1-4, 7-12, 15, 21-46, 48 and 49 are pending in the instant application. Claims 21-46 stand withdrawn from consideration as being directed to a non-elected invention. Claims 1-4, 7-12, 15, 48 and 49 are under consideration in the instant application.

Information Disclosure Statement:

The Examiner has considered documents NPL26 and NPL27, listed on IDS filed October 15, 2008. A signed copy of IDS is enclosed. The remainder of the references on said IDS has been lined through as they have been previously considered. A reference may appear only once on the face of the issued patent.

Withdrawn Rejections

The rejection of Claims 4 and 12 under 35 U.S.C. 101 is withdrawn in light of Applicants' amendment to the claims.

The rejection of Claims 4 and 12 under 35 U.S.C. 112, first paragraph (scope of enablement), is withdrawn in light of Applicants' amendment to the claims.

The rejection of Claim 3 under 35 U.S.C. 112, first paragraph (scope of enablement) is withdrawn in light of Applicants' amendment to the claims.

New/Maintained Rejections

35 U.S.C. § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Scope of Enablement

The rejection of Claim 11 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a virus comprising:

the multiple inducible gene regulation system of claim 9 wherein the system comprises a plurality of individually operable gene regulation systems wherein each individually operable gene regulation system comprises a polynucleotide comprising: an exogenous or endogenous gene; and a response element

does not reasonably provide enablement for:

the multiple inducible gene regulation system of claim 9 wherein the system comprises a plurality of individually operable gene regulation systems wherein each individually operable gene regulation system comprises one or more receptor complexes

is maintained for reasons of record and for reasons set forth below.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with these claims.

Applicants traverse this rejection (Remarks of 7 April 2009, page 19, last paragraph bridging page 20, 4th paragraph).

The reason for the traversal is:

Independent claim 9 has been amended herein to delete recitation of "a ligand." Accordingly, claim 11, which depends from claim 9 does not require that the

virus recited in claim 11 contains a ligand. As a result of the amendment of claim 9 herein, it is believed that the ground for this rejection has been obviated.

Applicant's arguments have been fully considered but are not found to be persuasive for the following reasons:

Claim 9 has been amended to delete recitation of "a ligand". Therefore, this part of the rejection has been withdrawn. However, claim 9 is drawn to gene regulation systems comprising one or more receptor complexes, that is, receptor protein complexes (claim 9 a)i) A, B, C). Therefore, claim 11, which is drawn to a virus comprising the multiple gene regulation system of claim 9 recite a virus comprising not only nucleic acids, but **receptor complexes (proteins)** as well.

The specification envisions the use of viral vectors to introduce and propagate nucleic acids in a host cell and organism. However, the disclosure provides no guidance to the skilled practitioner as to how to construct and utilize a virus comprising **a protein receptor complex** or how one is to introduce a vector comprising said protein receptor complex into a cell in such a way that these products would be propagated in and utilized by the cell. The working examples (Examples 1 and 2) teach transfection of cells with gene expression cassettes comprising nucleic acids and testing such cells for activity by exposing the cells to ligands such as ponasterone, and N-(2-ethyl-3-methoxybenzoyl)-N'-(3,5-dimethylbenzoyl)-N'-tert-butylhydrazine. There are no examples, working or prophetic, teaching construction of any vectors- comprising both **receptor proteins** and nucleic acids and utilizing such viral vectors in the methods disclosed in the specification.

The art teaches that viral vector systems comprising nucleic acids that encode proteins for the viral coat and enzymes necessary for viral integration into host chromosome. However, there are no teachings in the art of viral vector systems comprising receptor proteins and nucleic acids as recited in claim 11 of the instant invention nor are there teachings of how to make or use such vectors.

The rejection is thus maintained.

Written Description

The rejection of claims 1-4, 7-12, and 15 as failing to comply with written description requirement is maintained and now applied to newly submitted claims 48 and 49 for reasons of record and for reasons set forth below. The claim (s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are directed to a genus of an essentially unlimited scope of multiple gene regulation systems comprising two or more individually operable gene regulation systems, wherein each individual system operates independently of any other ("is orthogonal"). However, the only systems described are ones comprising two independent systems (Examples 1 and 2), a Lepidopteran/Dipteran and a Lepidopteran/Homopteran ecdysone receptor system. Applicant has not identified any particular structure of the ligand binding domains of the components of the gene regulation system that will provide the required specificity and uniqueness of binding between the ligand and the receptor for use in the claimed multiple orthogonal systems, but has identified the claimed systems solely by a function.

Applicants traverse the rejection (Remarks of 7 April 2009, page 21, 4th paragraph).

The reason for the traversal are:

The test for written description is whether the description provides that the inventors were in possession of the claimed invention. Here, that test is met, because the present application clearly establishes that the inventors were in possession of the presently claimed invention. Moreover, it is not necessary for an applicant to have reduced a claimed invention to practice, in order to have described the invention. See *Falkner v. Inglis*, 448 F.3d 1357, 1366 (Fed. Cir. 2006).

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Applicant's arguments have been fully considered but are not found to be persuasive for the following reasons:

Applicants have described multiple inducible systems comprising two independent systems (Examples 1 and 2), a Lepidopteran/Dipteran and a Lepidopteran/Homopteran ecdysone receptor system. The claims (1 and 9) are not limited to these systems or any systems with only two receptor expression cassettes, but are directed to multiple systems, comprising a plurality of individually operated gene regulation systems, i.e. having more than two, none of which have been further described. While applicants do not have to reduce the invention to practice, Applicants need to identify structure/ function relationships that will provide the required specificity and uniqueness of binding between the ligand and the receptor for use in the claimed multiple orthogonal systems, in order that the skilled artisan recognize that applicants were in possession of a genus of multiple expression systems.

Claims 48 and 49 are directed to multiple inducible gene regulation systems wherein said systems consist of two individually operable gene regulation systems. The claims encompass systems comprising the ligand binding domains (LBD) of any Group H nuclear receptor and the LBD of any nuclear receptor capable of forming a dimer with said Group H nuclear receptor LBD.

The specification teaches the genus of Group H nuclear receptors consist of numerous species including: ecdysone receptor, ubiquitous receptor (UR), Orphan receptor 1 (OR-1), steroid hormone nuclear receptor 1 (NER-1), RXR interacting protein-15 (RIP-15), liver x receptor .beta. (LXR.beta.), steroid hormone receptor like protein (RLD-1), liver x receptor (LXR), liver x receptor .alpha. (LXR.alpha.), farnesoid x receptor (FXR), receptor interacting protein 14 (RIP-14), and farnesol receptor (HRR-1) [paragraph 0148]. The second nuclear receptor ligand binding domain also comprises numerous species: a vertebrate retinoid X receptor ligand binding domain, an invertebrate retinoid X receptor ligand binding domain, an ultraspiracle protein ligand binding domain, and a chimeric ligand binding domain comprising two polypeptide fragments, wherein the first polypeptide fragment is from a vertebrate retinoid X

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receptor ligand binding domain, an invertebrate retinoid X receptor ligand binding domain, or an ultraspiracle protein ligand binding domain, and the second polypeptide fragment is from a different vertebrate retinoid X receptor ligand binding domain, invertebrate retinoid X receptor ligand binding domain, or ultraspiracle protein ligand binding domain [paragraph 0158]. Thus, newly submitted claims 48 and 49 are also directed to a genus of multiple gene regulation systems comprising numerous species of two individually operable gene regulation systems, wherein each individually system operates independently of any other ("is orthogonal").

As stated above and in previous Office Actions, Applicants have described multiple inducible systems comprising two independent systems (Examples 1 and 2) (two species of the claimed genus), a Lepidopteran/Dipteran and a Lepidopteran/Homopteran ecdysone receptor system.

However, claims 48 and 49 encompass multiple systems, comprising a plurality of individually operated gene regulation systems which have not been further described. The skilled artisan would not recognize that applicants were in possession of a genus of multiple expression systems. Applicants have not identified any particular chemical structure that will provide the required specificity and uniqueness of binding between the ligand and the receptor for use in the claimed multiple orthogonal systems, but have identified the claimed systems solely by a function.

Pages 40-43 of the specification [paragraphs 0204-0240], disclose complex, art-recognized methods of searching for specific ligands and screening for novel cognate LBDs. The structures of ligands presented on page 40, as potential chemotypes ideal for use as ligands, comprise a natural ecdysteroid and a known diacylhydrazine. These compounds appear to be cross-interactive across insect species, which is contrary to that required by the claimed invention, that the multiple systems be orthogonal. Applicants teach that "an orthogonal ligand/receptor set does not exist within these two structural families". This is certainly not evidence of possession but indicates that to achieve the goal of a multiple, orthogonal gene regulation system, as broadly claimed, further experimentation is required (page 40, lines 8-15, paragraph 0205).

Thus, applicants have not disclosed any additional molecules as ligands nor have they identified any particular cognate LBDs. The methods outlined act as an invitation to design and discover which ligands-receptor pairs may work as the multiple gene regulatory systems of the instant invention.

Applicants' teachings are an invitation to experiment to design, identify and isolate appropriate receptor/ligand pairs which act orthogonally; the disclosure does not provide evidence that Applicants were in possession of such. Possession may not be shown by merely describing how to obtain possession of members of the claimed genus or how to identify their common structural features.

An invitation for others to discover a representative number of species with known or disclosed correlation between function and structure of the polynucleotides or polypeptides of gene modulation systems or by a combination of such identifying characteristics does not reasonably provide one of skill in the art with sufficient information to reasonably visualize or predict which ligand/receptor pairs would be encompassed by the claims. Possession may not be shown by merely describing how to obtain possession of members of the claimed genus or how to identify their common structural features. See *University of Rochester*, 38 F.3d at 927, 69 USPQd at 1895. Without a correlation between structure and function the claim does little more than define the claimed invention by function. That is not sufficient to define a genus because it is only an indication of what the gene or ligand does, rather than what it is, see, *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406.

Applicants are not in possession of the claimed genus of "multiple inducible gene modulation system" and thus, the current claims do not comply with the requirement for written description under 35 USC 112, first paragraph.

Therefore, the Lepidopteran/Dipteran and Lepidopteran/Homopteran receptor schemes (of the Group H family of receptors) but not the full breadth of the claims meet the written description provision of 35 U.S.C. 112, first paragraph.

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Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 115).

Conclusions:

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHULAMITH H. SHAFER whose telephone number is (571)272-3332. The examiner can normally be reached on Monday through Friday, 8 AM to 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath Rao, Ph.D. can be reached on 571-272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Shulamith H. Shafer/ Ph.D.

Examiner, Art Unit 1647

/Manjunath N. Rao /

Supervisory Patent Examiner, Art Unit 1647